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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/680,950
Filing Date: October 08, 2003
Appellant(s): LANGLEY ET AL.

Michael Curtis
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 7 August 2008 appealing from the Office action mailed 18 January 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct. No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,179,801	HOLMES	01-2001
5,980,465	ELGAS	11-1999
6,730,054	PIERCE	05-2004

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-12, 14-15, 17-40, 42-45, 47-50, 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,179,801 to Holmes et al in view of US 5,980,465 to Elgas.

In the specification and figures, Homes discloses the method substantially as claimed by Applicant. With regard to claims 25-27, Holmes discloses a blood processing apparatus and method that comprises the steps of entering patient data into a control screen to calculate the donor's total blood volume and using the total blood volume in the determination of various parameters of the apheresis procedure (see column 56, lines 61 to column 57, line 2). Holmes specifically discloses that blood inlet pump 1030 is operated according to parameters stored in blood component separation device 6, which receives the patient parameters described above (see column 27, lines 15-25). Therefore, the removal of blood from the patient via removal pump 1030 is performed in

a manner derived from the predetermined operating protocol stored in apheresis machine 6, which operates, in part, on patient blood volume data. Similarly, Homes discloses that the return rate of the blood return submode via return pump 1090 is established by blood component separation device 6 according to a predetermined protocol (see column 27, lines 15-25).

Holmes fails to disclose the step of adjusting a removal and/or flow rate during the blood processing procedure based on the total blood volume. However, Elgas discloses a method for detecting changes in patient's blood volume during extracorporeal treatments. Elgas discloses that maintaining a patient's total blood volume during extracorporeal procedures is clinically significant to maintaining physiological status, teaches that increasing fluid flow to the patient in the event of total blood volume decrease is a good way to maintain that status quo (see column 1, lines 31-57). Such a disclosure reasonably suggests to one of ordinary skill in the art other steps, such as adjusting blood withdrawal rate, would be within the range of reasonable steps taken to maintain the patient's total blood volume. It would have been obvious to one having ordinary skill in the art at the time of invention to use the suggestion of the Elgas disclosure with regard to maintaining patient total blood volume through fluid flow rate adjustments in the apheresis procedure disclosed by Holmes in order to maintain physiological status quo of the patient, as taught by Elgas. Accordingly, the combination of the Holmes and Elgas references suggest the method claimed by Applicant.

With regard to Applicant's claims drawn to "systematic" variance of flow rates (eg, claims 1, 23), Holmes clearly discloses that the apheresis system 6 varies the flow

rates based on a predetermined operating scheme (see column 27, lines 15-25, column 56, lines 60-67). Since the system controls such variations, Examiner considers flow rates adjusted by the apheresis system 6, including elimination of flow at the end of the processing period (see column 28, lines 40-44) to correspond to Applicant's "systematic" variations, since the variations are derived from the system

With regard to claims 12, 40, and 67, Holmes specifically discloses that blood is removed and returned through patient access 30 and needle 32 (see FIG 2A).

With regard to claims 42, 43, 21, and 22, Holmes discloses that the blood processing method includes a blood removal submode and a blood return submode that repeat sequentially for a predetermined amount of time (see column 28, lines 40-44).

With regard to claims 44, 45, 14, and 15, Holmes specifically discloses that the blood processing procedure may be used to separate a patient's whole blood via a centrifuge into constituent components, wherein one or more components are retained by the system (corresponding to Applicant's claimed collect component) and the undesired components are returned to the patient (see column 1, lines 16-25; see also column 8, lines 20-60 for density centrifuge).

With regard to claims 47-50 and 17-20, Holmes discloses that the collected component may comprise red blood cells, white blood cells, platelets, or plasma (see column 1, lines 16-25).

With regard to claim 1, Holmes discloses that the return pump 1090 may be started and stopped according to the operating parameters of the system, thereby varying the rate of fluid return to the patient (see column 27, lines 25-35).

With regard to claim 2, Holmes discloses that the return pump 1090 is stopped after the completion of the return time (see, for example, column 28, lines 40-43). Such a stoppage represents a decrease in the return flow rate, thereby meeting the limitations of the claim.

With regard to claim 11, Holmes discloses that the blood removal submode may be stopped in response to signals from the blood separation device 6, thereby halting blood removal pump 1030 (see column 27, lines 10-15). Such stopping of the blood pump is considered by the examiner to vary the rate of the removal, meeting the limitations of the claim.

With regard to claims 3, 8, 9, and 10, Holmes specifically discloses in column 56, lines 61-67, that patient data such as patient blood volume are used to establish the operating parameters of the apheresis device 6, thereby regulating the disclosed blood processing method. In column 27, lines 15-25, Holmes teaches that the volume transfer rate of blood flow is variable based on a "predetermined protocol" of the apheresis machine 6. Accordingly, this flow rate is regarded as a result-effective variable (see also at least column 28, lines 44-67 for discussion of variable flow rates). It has been held that the optimization of a result-effective variable involves only routine skill in the art. See MPEP 2144.05. In the instant case, Examiner considers the flow rates claimed by Applicant (eg, increasing, decreasing, exponentially decreasing, or linearly varying) to be a result-effective variable (the adjustment of which does not patentably distinguish over the prior art of record) that may be controlled by collected and calculated patient data, thereby meeting the limitations of the claims.

With regard to claims 4-7, 30-31, and 34-39, Applicant claims to establish a return flow rate based on a specific equation. As noted above, Holmes discloses that the flow rate is recognized to be a result-effective variable. These claims establish a method for setting/optimizing various flow rates via the selection of variable/optimal parameters. Absent a disclosure that Applicant's claimed equations provide a significant advantage over the prior art's calculation, Examiner considers the selection of such variable parameters to be mere optimization of a result-effective variable through routine experimentation. Holmes specifically teaches that such parameters may be selected as desired by the operator and blood handling procedure (see, generally, columns 27-28). Accordingly, as previously noted, the optimization of a variable flow rate is not considered to patentably distinguish Applicant's invention from the prior art of record. See MPEP 2144.05.

With regard to claim 23, Holmes discloses that the blood removal submode may be stopped in response to signals from the blood separation device 6, thereby halting blood removal pump 1030 (see column 27, lines 10-15). Such stopping of the blood pump is considered by the examiner to vary the rate of the removal, meeting the limitations of the claims. With regard to Applicant's claim limitation drawn to the ability of the method to reduce vessel infiltration, Applicant discloses that such infiltration is generally a result of large pressure fluctuations while withdrawing or returning fluid to the patient's blood vessel. Holmes specifically discloses that pressure sensor 1200 senses negative and positive pressure changes in the removal tubing 22 and return tubing 26. The pressure signals are conveyed to the separation device 6, which controls

the operation of removal pump 1030 and return pump 1090 (and thereby the flow rate) to maintain predetermined fluid pressures during the procedure (see column 27, lines 36-61). Holmes discloses that the pressure is controlled, which necessarily controls what Applicant discloses is the cause of infiltration. It follows naturally that in controlling the pressure, the rate of infiltration is also controlled, thereby meeting the limitations of the claim.

With regard to claim 24, while increasing the removal flow rate is regarded as an optimization of a result-effective variable found in the prior art (see rejection above), Holmes specifically discloses that the blood processing method includes a blood removal submode and a blood return submode that repeat sequentially for a predetermined amount of time (see column 28, lines 40-44).

With regard to claims 28 and 29, as previously noted, Holmes uses the total blood volume of the patient in the determination of various parameters of the apheresis procedure (see column 56, lines 61-67). Furthermore, Holmes appears to suggest that such parameters include the withdrawal and return flow rates (see, generally, columns 27-28). Therefore, the linear correlation of the flow rate and increase of the flow rate found in the claims would be a matter of optimizing a result-effective variable found in the prior art. It has been held that the optimization of a result-effective variable involves only routine skill in the art. See MPEP 2144.05. In the instant case, Examiner considers the flow rates claimed by Applicant (eg, increasing, decreasing, exponentially decreasing, or linearly varying) to be a result-effective variable (the adjustment of which

does not patentably distinguish over the prior art of record) that may be controlled by collected and calculated patient data, thereby meeting the limitations of the claims.

With regard to claims 32 and 33, Applicant attempts to claim a method for determining blood volume with a formula based on patient sex, height, and weight. Holmes discloses that his procedure comprises a method for determining blood volume based on patient sex, height, and weight (see column 56, lines 48-67). Without a disclosure of how Applicant's formula improves the determination of blood volume from that found in the prior art, Examiner considers the claimed formula to be merely a matter of optimizing the manner in which each procedure arrives at the patient's total blood volume. It has been held that the optimization of a result-effective variable involves only routine skill in the art. See MPEP 2144.05. In the instant case, Examiner considers Applicant's selection of variable coefficients in an equation to be a matter of routine experimentation that optimizes accurate determination of patient blood volume.

Claims 13, 16, 41, 46, 51-53, and 56-66, and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,179,801 to Holmes et al in view of US 5,980,465 to Elgas, further in view of US 6,730,054 to Pierce et al.

In the specification and figures, Holmes and Elgas suggest the method substantially as claimed by Applicant (see rejection above) with the exception of two needles to draw and return blood, an elutriation centrifugation, and a recirculation step.

With regard to claims 13 and 41, Pierce discloses a blood processing system that draws blood from a patient based on patient parameters such as patient blood volume,

separates the blood into components, and returns the unused component to the patient (see column 1, lines 50-55, column 3, lines 57-63, column 12, lines 54-61). Pierce discloses that the system may comprise either a single needle blood collection system or a double needle system (see column 2, lines 65-67). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to perform the blood processing procedure suggested by Holmes and Elgas with a two needles as disclosed by Pierce, since Pierce teaches that single and double needle processing systems are interchangeable.

With regard to claims 51 and 53, Pierce discloses a recirculation procedure that adds separated PRP to entering whole blood in order to maximize the separation of RBC and PRP to prevent contamination with RBC (see column 8, lines 54-65). As such, Pierce discloses the steps of conducting removed, anticoagulated WB through system 10, wherein the system collects RBC and PRP (see column 8, lines 29-32). The system collects a portion of the PRP for further processing (corresponding to Applicant's first portion), and recirculates a portion of the PRP through the system to combine with WB for increased separation efficiency (wherein the recirculated PRP corresponds to Applicant's claimed second portion) (see column 8, lines 29-60). During this mode, the controller returns unused RBC and PPP (corresponding to Applicant's third component) to the patient. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to add a recirculation step as disclosed by Pierce to the blood separation and collection procedure as suggested by Holmes and Elgas, in order to provide maximal separation of RBC and PRP, as taught be Pierce.

With regard to claims 16, 46, and 56, Pierce's recirculation of PRP into the collected WB creates a secondary elutriation process that increases the separation of platelets from WB by adding extra PRP as a washing fluid to provide maximal separation of RBC and PRP. Accordingly, Pierce discloses a blood separation procedure that uses both density centrifugation and elutriation to separate the desired blood components, meeting the limitations of the claims. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use a washing/elutriation process as disclosed by Pierce in the blood processing procedure suggested by Holmes and Elgas, in order to increase separation efficiency, as taught be Pierce.

With regard to claim 52, Holmes discloses that the blood processing method includes a blood removal submode and a blood return submode that repeat sequentially for a predetermined amount of time (see column 28, lines 40-44).

With regard to claims 63-66, Holmes discloses that the collected component may comprise red blood cells, white blood cells, platelets, or plasma (see column 1, lines 16-25).

With regard to claims 57 and 58, the prior art discloses both a removed blood portion and a recirculated blood portion, each of which necessarily has a hematocrit value. This weighted average of the hematocrit values necessarily varies with the amount of blood supplied to the processing device. Pierce teaches that hematocrit values are calculated based on flow considerations (see column 7, lines 14-20). Accordingly, variation of flow conditions necessarily varies hematocrit values, creating a

result-effective variable. As understood in the art, hematocrit values of separated portions may vary with variations in flow conditions that alter the efficiency of separation, which may result in higher or lower hematocrit concentration in a recirculated portion. Since hematocrit value is based on flow conditions, the flow conditions may be manipulated in to create the hematocrit ratio claimed by applicant.

Pierce does not provide any limitation to the amount of fluid supplied to the withdrawn blood in the recirculation loop, but does disclose that the amount is sufficient to establish desired conditions in the blood separation system. Therefore, Pierce suggests that the amount of recirculated portion combined with the removed blood may be selected to maximize a desired result—efficient separation of RBC and PRP. It has been held that the optimization of a result-effective variable involves only routine skill in the art. See MPEP 2144.05. In the instant case, the portion of the recirculated flow is selected to provide the result of maximum separation of RBC and PRP.

With regard to claims 59-62 and 68, as noted above, each portion of blood necessarily has a hematocrit value, and the draw and return cycles each have a rate (see rejections above). Applicant uses an equation to set the duration of each cycle. Both Holmes and Pierce teach that the method comprises draw and return cycles. Broadly defined, a cycle comprises an interval of time (see Merriam-Webster's Collegiate Dictionary, 10th Ed., 2001). All the values used in the determination of $F_{c\,max}$ in the claimed equation are demonstrated by the prior art to be variable. It has been held that the optimization of a result-effective variable involves only routine skill in the art. See MPEP 2144.05. In the instant case, the duration of the draw and return cycles

are varied in order to provide a sufficient amount of time to provide blood to the separation system and to return components to the donor, respectively. (see Pierce, column 7, lines 45-50). Accordingly, Examiner considers the selection of such variable parameters to be mere optimization of a result-effective variable through routine experimentation.

(10) Response to Argument

With regard to claims 1-12, 14-15, 17-40, 42-45, 47-50, and 67:

Applicant argues that Holmes in view of Elgas does not suggest the limitations of claims 25-27, along with its dependent claims. Specifically, Applicant argues that Holmes in view of Elgas does not disclose adjusting the blood removal rate or return rate based on the patient's total blood volume.

Applicant argues, and Examiner agrees, that Holmes doe not adjust blood removal flow rate or blood return flow rate *based on the total blood volume* of the patient. However, Holmes *does* teach that removal and flow rates are adjusted (via pump speed of variable speed pumps) based on a predetermined apheresis protocol (see Holmes column 27, lines 15-25) and operating parameters (see Holmes column 28, lines 44-67). The apparatus disclosed by Holmes uses patient parameters to calculate total patient blood volume (see Holmes column 56, line 42 to column 57, line 6), which, in turn, is utilized to determine various parameters of the apheresis procedure such as blood inlet rate and outlet rate (see Holmes column 53, lines 55-60, column 27, lines 15-25). Accordingly, it is the position of the Examiner that Holmes teaches a

method in which the blood inlet rate and outlet rate are determined by various patient parameters, including patient blood volume, and are adjustable during the procedure based on real-time sensed measurements, such as pressure. As such, Holmes teaches adjustable flow rates and the importance of total patient blood volume.

Holmes does not disclose that the inlet and outlet blood flow rates are adjusted *during* the procedure *based on total patient blood volume.* However, Elgas discloses a method for detecting changes in patients' total blood volume *during* an extracorporeal treatment. Applicant notes that Elgas teaches the administration of outside IV fluids , not adjustment of blood withdrawal and return rates, to maintain the patient's total blood volume, which is clinically significant to the patient's status. The Examiner agrees with Applicant's assessment. However, the Examiner notes that Elgas teaches that blood is withdrawn and returned via a variable-speed roller pump which may be accurately controlled, which suggests adjustability of flow rate (see Elgas column 1, lines 20-51). Elgas further discloses that a drop in blood volume may be solved by increasing IV fluid flow rate or blood transfusion, and that the system comprises a blood reservoir 20. It follows naturally that if a patient's blood volume changes, one using the Elgas device would adjust variable speed pump 22 to adjust the blood withdrawal and return rates based on such a measurement. The Examiner is relying on the Elgas reference to teach a) the criticality of patient blood volume and b) that adjusting fluid flow rates is a recognized way of responding to changes in blood volume.

Holmes teaches that blood withdrawal and return rate may be adjusted based on patient parameters according to a predetermined apheresis protocol, but does not teach

that total blood volume is a measurement made in real time. Elgas teaches that a real time measurement of patient blood volume during an extracorporeal treatment may be used to adjust a fluid flow rate. Accordingly, it is the position of the Examiner that taken together, the references reasonably suggest the process of adjusting blood withdrawal and return rates in an extracorporeal procedure based on total patient blood volume.

Applicant argues that the variable speed roller pump disclosed by Elgas is not capable of varying blood withdrawal speed, since the blood pulled by the pump comes from variable volume reservoir 20. However, if the reservoir comprises a closed container, when it is empty, the pump will create a vacuum in the direction of inlet lines 17, 18, thereby allowing adjustments in the speed of the pump affect blood withdrawal rates.

Applicant argues that since neither reference teaches the adjustment of blood removal or return rates based on total blood volume, the references cannot be combined to teach the method claimed by Applicant. However, the Examiner asserts that Holmes teaches a method whereby blood withdrawal and return rates are indirectly affected by total blood volume, as discussed above in the creation of the apheresis protocol. Elgas teaches that total blood volume may be used to control a different extracorporeal procedure. Together, the two teachings provide the suggestion that one may use a real-time total blood volume measurement (such as taught by Elgas) to generate and later control an apheresis protocol, which involves the adjustment of blood withdrawal and return rates (as taught by Holmes). Accordingly, it is the position of the

Examiner that, taken together, the references reasonably suggest the method claimed by Applicant.

Applicant argues that adjusting the fluid return and withdrawal rates in the apparatus disclosed by Elgas might have disastrous consequences for the patient. The Examiner is not proposing such a scenario, and relies on the Elgas reference to teach how a real-time measurement of total blood volume may be used to adjust a pump speed (such as IV pump 16) during a particular surgical procedure.

Applicant further argues that the methods taught by Elgas are not suitable for preventing blood flow infiltration due to access vessel pressure changes, since administering an outside fluid would exacerbate the problem. However, the Examiner is not proposing such a scenario, and relies on the Elgas reference to teach how a real-time measurement of total blood volume may be used to adjust a pump speed (such as IV pump 16) during a particular surgical procedure.

With regard to claims 1, 11, and 23:

Applicant argues that the step of "systematically varying" the removal rate and return rate specifically refers to substantially linear, exponential, logarithmic, or quadratic, as defined in page 19 of Applicant's specification. The Examiner recognizes Applicant's attempt to define the variations, but notes that Applicant discloses that certain "parameters such as return flow rate, removal flow rate... *may be* systematically varied by substantially linear...exponential...logarithmic...quadratic variations." (See Applicant's specification at page 19, lines 8-14). Applicant's use of "may be" language is

open ended, indicating that other variations are permissible within the scope of the defined "systematically varying." Accordingly, it is the position of the Examiner that the broad interpretation of "systematically varying" provided by the Examiner meets the limitations of the claims.

With regard to claims 3, 8, 9, and 10 as well as 4-7, 30-31, and 34-39:

Applicant argues that total blood volume has not been recognized as a result-effective variable which achieves a recognized result. Examiner respectfully disagrees. Elgas suggests that adjustment of total patient fluid volume may be accomplished via IV infusion, but also discloses a variable speed pump that removed fluid from the patient, suggesting that fluid removal rate may also be used to control patient fluid volume. Taken together, the references reasonably suggest that manipulation of fluid removal and/or return rates are variables, that when manipulated, control total patient fluid volume. Accordingly, the references suggest that variation of the fluid removal and return rates are result-effective variables that may be controlled by collected and calculated patient data, thereby meeting the limitations of the claims.

Applicant argues that the variable speed roller pump disclosed by Elgas is not capable of varying blood withdrawal speed, since the blood pulled by the pump comes from variable volume reservoir 20. However, if the reservoir comprises a closed container, when it is empty, the pump will create a vacuum in the direction of inlet lines 17, 18, thereby allowing adjustments in the speed of the pump affect blood withdrawal rates.

With regard to claims 59-62 and 68:

Applicant argues that the Pierce reference fails to overcome the deficiencies of Holmes and Elgas. Examiner respectfully disagrees. Holmes and Elgas suggest the method as claimed by Applicant. With regard to claims 57-58, Applicant merely claims that a first portion of fluid and a second portion of fluid comprise a particular hematocrit ratio, but does not disclose or claim what steps are taken in the method to establish such a ratio. Pierce teaches that hematocrit values are calculated based on flow considerations (see column 7, lines 14-20). Accordingly, variation of flow conditions necessarily varies hematocrit values, creating a result-effective variable. As understood in the art, hematocrit values of separated portions may vary with variations in flow conditions that alter the efficiency of separation, which may result in higher or lower hematocrit concentration in a recirculated portion. Since hematocrit value is based on flow conditions, the flow conditions may be manipulated in to create the hematocrit ratio claimed by applicant. Examiner is not asserting that hematocrit ratios are used to control the efficacy of the blood separation device, but that the variation of flow rates and combination of recirculated fluid with removed blood, as disclosed by Pierce, amounts to a manipulation of a result-effective variable (flow rate), wherein the efficiency of separation comprises the result. Such manipulation may arrive at the hematocrit ratios claimed by applicant, suggesting the limitations of the claims.

With regard to claims 59-62 and 68, Pierce discloses that hematocrit values are affected by flow conditions, which include the duration of the draw and return cycles.

Since the duration of the draw cycle affects the length of time the withdrawn blood is processed, it necessarily affects the hematocrit value of both the collected portion and the recirculated portion. The duration of the return cycle affects the amount of fluid and the frequency at which the fluid is returned to the patient, affecting the hematocrit of the whole blood. Accordingly, the duration of the draw and return cycles necessarily affects the hematocrit values, and therefore the ratio between the hematocrit of the whole blood, collected portion, and the recirculated portion. Accordingly, the manipulation of the duration of the draw and return cycles amounts the manipulation of a result-effective variable (the duration of each cycle), wherein the efficiency of separation comprises the result.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Leslie R. Deak/

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/Tatyana Zalukaeva/

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/Heather Shackelford/

OPQA